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Original Article

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Anxiety Depression and Somatosensory Amplification in Patients Consulting Psychiatry from Different Clinics

Psikiyatriye Farklı Kliniklerden Konsultasyon ile Gelen Hastaların Anksiyete Depresyon ve Somatosensoryal Amplifikasyonu

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ABSTRACT

Objective: Psychiatric consultation is often requested in hospitals for patients whose complaints cannot be fully explained by physical illness and who are struggling with the psychological effects of their condition. This study aimed to assess the anxiety, depression, and somatosensory amplification (SSA) levels of patients referred to psychiatry outpatient clinics from various departments and to compare them with those of healthy controls.

Material and Methods: A total of 201 individuals participated in the study, comprising 169 consultation patients and 32 controls. Among the consultation group, 43 patients were referred from neurology, 48 from gastroenterology, 38 from cardiology, and 40 from internal medicine departments. The demographic information form, the Hospital Anxiety and Depression (HAD) scale, and the SSA scale were administered to the patient group. The control group received the demographic form and the SSA scale, but not the HAD scale. Statistical analyses were conducted using a one-way ANOVA.

Results: A significant difference was found in the HAD-anxiety scores among the consultation groups (F=5.812, p=0.001), with the Cardiology Consultation Group showing higher mean anxiety levels compared to the other groups. No significant difference was observed in the HAD-depression scores among the groups (p=0.792); however, the mean scores in all groups exceeded the clinical cut-off value (7-8). For the SSA scores, a significant difference was observed among the consultation groups, primarily due to the elevated scores in the Gastroenterology Consultation Group (F=1.278, p=0.014). When comparing all consultation groups with the control group, a statistically significant difference was found (F=82.893, p=0.000).

Conclusion: Patients referred for psychiatric consultation exhibited high levels of SSA, depression, and anxiety symptoms. Particularly, patients referred from internal medicine departments may require more detailed psychiatric evaluation.

Keywords: Psychiatric consultation, depression, anxiety, somatosensory amplification

ÖZ

Amaç: Psikiyatrik konsültasyon, hastanelerde fiziksel hastalıkla açıklanamayan, oransız yakınmaları olan ve hastalığının olumsuz etkileri ile savaşan hastalar için istenmektedir. Psikiyatri polikliniklerine konsültasyon ile en çok başvuru dahiliye, gastroenteroloji, kardiyoloji, nöroloji gibi dahili dallardan olduğu bilinmektedir. Bu çalışmada amaç psikiyatri polikliniğine çeşitli polikliniklerden gelen hastaların anksiyete, depresyon ve somatosensoriyel amplifikasyon (SSA) değerlerini ölçülmesi ve birbirleriyle ve sağlıklı bireylerle karşılaştırılmasıdır.

Gereç ve Yöntemler: Çalışmaya konsültasyonla gelen 169 hasta ve 32 kişilik kontrol grubu olmak üzere toplamda 201 kişi katılmıştır. Konsültasyonla gelen grubun 43 kişi nörolojiden konsültasyonla gelen, 48 kişi gastroenterolojiden konsültasyonla gelen, 38 kişi kardiyolojiden konsültasyonla gelen ve 40 kişi ise dahiliyeden konsültasyonla gelen grup olarak gönderilmiştir. Hasta grubuna demografik veri formu, Hastane Anksiyete Depresyon (HAD) ölçeği ve SSA ölçeği verilmiştir. Kontrol grubuna HAD ölçeği dışındaki demografik veri formu ve SSA ölçeği verilmiştir.

Bulgular: Konsültasyonla gelen gruplar arasında HAD-anksiyete değeri açısından one-way ANOVA testi ile anlamlı fark saptanmıştır (F=5,812, p=0,001). Kardiyolojiden Konsültasyonla Gelen Grubunun anksiyete ortalaması diğer gruplara oranla yüksek olarak bulunmuştur.

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ÖZ

Gruplar arasında HAD-depresyon testi için fark bulunamamıştır (p=0,792). Ancak tüm grupların ortalaması bu test için kesim noktası üzerinde olup kesim noktası (7-8) yüksek olarak bulunmuştur. SSA ölçeği açısından tüm konsültasyon grupları karşılaştırıldığında istatistiksel olarak fark bulunmuştur. Fark Gastroenterolojiden Konsültasyonla Gelen Grubunun yüksek değerlerinden kaynaklandığı düşünülmüştür (F=1,278, p=0,014). Tüm konsültasyon grupları ile kontrol grubu arasındaki fark istatistiksel olarak anlamlıdır (F=82,893, p=0,000).

Sonuç: Sonuç olarak psikiyatri polikliniklerine konsültasyonla gelen hastalarda depresyon ve anksiyete belirtilerinin yüksek oranda bulunduğu SSA yüksek değerlerde olduğu anlaşılmıştır. Özellikle dahili polikliniklerden gelen hastaların daha ayrıntılı değerlendirilmesine gerek olduğu düşünülmektedir.

Anahtar Kelimeler: Psikiyatrik konsültasyon, depresyon, anksiyete, somatosensoriyel amplifikasyon

INTRODUCTION

In general hospitals, there are patients with complaints that are unexplained or disproportionate to their physical condition, therefore struggling with the negative effects of their illness. Psychiatric consultation is requested for these patients. The aim of consultations is not only to make a psychiatric diagnosis but also to reveal the connection and interaction between the physical and mental domains. It is known that the most common consultations to psychiatry outpatient clinics are from internal medicine, gastroenterology, cardiology, neurology, and physiotherapy, and rehabilitation. It has been reported that anxiety disorders and depression are more common in patients referred to psychiatry outpatient clinics for consultation (1).

In addition, the presence of physical illness causes the person to focus more attention on their body. These different sensations and scant evidence can lead to panic symptoms. In 1992, Barsky described somatosensory amplification (SSA) amplification who believe they have a physical illness tend to focus on their somatic sensations and experience them as harmful and disturbing (2). The anterior cingulate cortex, insula, amygdala, hippocampal formation, and striatum are some of the areas identified for SSA. Clinical symptoms are attributed to neurobehavioral disturbances in one or more areas. SSA can be caused in part by stress, but also by abnormal neuroplasticity of the brain and the neuromodulatory effects of inflammation (3).

This study aimed to measure anxiety, depression, and SSA values of patients coming from various psychiatry outpatient clinics and to compare them with healthy individuals.

MATERIALS and METHODS

The study group consisted of 169 patients referred for psychiatric consultation. Among these, 43 patients were included in the Neurology Consultation Group (NCG), 48 in the Gastroenterology Consultation Group (GCG), 38 in the Cardiology Consultation Group (CCG), and 40 in the Internal Medicine Consultation Group (IMCG). Thirty-two healthy volunteers were included as the control group.

Patients in the NCG presented with complaints such as non-epileptic fainting, headaches, muscle pain, and nonspecific numbness in the arms and legs. Patients in the GCG were referred for abdominal pain, indigestion, diarrhea, constipation, and bloating. Patients in the CCG presented with palpitations, chest pain, and shortness of breath. Patients in the IMCG reported symptoms of weakness, fatigue, anorexia, nausea, and abdominal pain; however, no physical illness was diagnosed following comprehensive clinical evaluations.

This cross-sectional study was conducted at the psychiatry outpatient clinics of Adana City Hospital and Kozan State Hospital. Written informed consent was obtained from all participants, including those in the control group. The control group was selected to be comparable to the patient groups in terms of age, gender, and marital status.

The patient group completed a demographic data form, the Hospital Anxiety and Depression (HAD) scale, and the SSA scale. The control group completed the demographic form and the SSA scale, but did not complete the HAD scale.

Hospital Anxiety and Depression Scale

The HAD is a four-point Likert-type scale developed by Zigmond and Snaith (4) to assess the risk and severity of anxiety and depression in patients. It consists of 14 items, with odd-numbered questions assessing anxiety and even-numbered questions assessing depression. The Turkish validity and reliability study of the scale was conducted by Aydemir (1), demonstrating its reliability for screening depression and anxiety symptoms in patients with physical illness (5).

Somatosensory Amplification Scale

The SSA is a 10-item Likert-type scale developed by Barsky et al. (2) to measure sensitivity to uncomfortable bodily sensations. Higher scores indicate an exaggerated perception of bodily sensations. The Turkish version of the scale has been validated (6).

Statistical Analysis

The Kolmogorov-Smirnov test was used to assess the normality of data distribution. Since the data were normally distributed and there were more than two groups, one-way ANOVA was used for comparisons of continuous variables. The chi-square test was used for comparisons of categorical variables. Statistical analyses were performed using SPSS version 22.0. A p value of less than 0.05 was considered statistically significant.

RESULTS

A total of 201 people, consisting of 169 patients and 32 controls, participated in the study. The mean and standard deviations of study group age were as follows: NCG group, 35.88+9.38; GCG group, 35.68+8.48; IMCG group, 38.65+10.83; the control group, 34.90+8.43. No statistical difference was found between the groups. Significant statistical differences gender, education, and occupation as sociodemographic data was found by Pearson's chi-square test. The difference was caused by the fact that the majority of our groups were female, with a low education level and professionally unemployed, as housewives (gender: chi-square= 22.25, p=0.000, education: chi-square= 25.82, p=0.011, occupation: chi-square= 36.01, p=0.000). There was no difference between the groups in terms of marital status (chi-square=8. 38, p=0.387). All sociodemographic data and the numbers and percentages of the groups are presented in Table 1. A significant difference was found between the consultation groups in terms of HAD-A value by a one-way ANOVA test (F=5.812, p=0.001). The mean anxiety level of the CCG group was found to be higher than any of the other groups. There was no difference between the groups in the HAD depression test (p=0.792). However, the mean of all groups was above the cut-off point for this test (cut-off point=7-8) and was found to be high. When all consultation groups were compared in terms of the SSA scale, a statistical difference was found. The difference was thought to be due to the high values of the GCG group (F=1.278, p=0.014). These values are shown in Table 2. The difference between all consultation groups and the control group was determined using a one-way ANOVA test. The difference was statistically significant (F=82.893, p=0.000). The results are in Table 3.

Table 1. Demographic data for the five groups

Groups	NCG (n=43)	GCG (n=48)	CCG (n=38)	IMCG (n=40)	Control (n=32)	Statistics
Age (Mean ± SD)	35.88±9.38	35.68±8.48	36.31±10.83	38.65±10.83	34.90±8.43	F=1.765 p=0.138
Women	38 (88.38%)	39 (81.25%)	20 (52.64%)	31 (88.89%)	27 (81.49%)	χ^2=22.25 p=0.000
Men	5 (11.62%)	9 (18.75%)	18 (47.36%)	4 (11.11%)	5 (18.51%)	
Primary	17 (39.53%)	11 (22.91%)	18 (47.36%)	22 (55.00%)	13 (40.62%)	
Secondary	4 (9.30%)	16 (33.33%)	7 (18.42%)	4 (10.00%)	4 (12.50%)	χ^2=25.82 p=0.011
Highschool	13 (30.23%)	17 (35.41%)	5 (13.15%)	11 (27.50%)	9 (28.12%)	
University	9 (20.93%)	4 (8.33%)	8 (21.05%)	3 (7.50%)	6 (18.75%)	
Unemployed-housewife	35 (81.39%)	30 (62.50%)	25 (65.78%)	37 (92.50%)	23 (71.87%)	
Worker	6 (13.95%)	6 (12.50%)	13 (34.21%)	2 (5.00%)	7 (21.87%)	χ^2=36.01 p=0.000
Officer	2 (4.65%)	12 (25.00%)	0 (0.00%)	1 (2.50%)	2 (6.25%)	
Married	27 (62.79%)	31 (64.58%)	32 (84.21%)	29 (72.05%)	25 (71.87%)	
Single	12 (27.90%)	10 (20.08%)	5 (13.15%)	9 (22.50%)	7 (21.87%)	χ^2=8.380 p=0.387
Widowed-divorced	4 (9.30%)	7 (14.58%)	1 (2.63%)	2 (5.00%)	2 (6.25%)	

NCG: Neurology Consultation Group, GCG: Gastroenterology Consultation Group, CCG: Cardiology Consultation Group, IMCG: Internal Medicine Consultation Group

Table 2. HAD-A HAD-D data of the groups

Groups	NCG (n=43)	GCG (n=48)	CCG (n=38)	IMCG (n=40)	Statistics
HAD-A (Mean ± SD)	11.44±4.63	12.14±3.16	14.63±2.40	12.32±3.58	F=5.812 p=0.001
HAD-D (Mean ± SD)	9.60±4.55	9.22±3.78	9.07±3.15	9.87±3.91	F=0.392 p=0.792

NCG: Neurology Consultation Group, GCG: Gastroenterology Consultation Group, CCG: Cardiology Consultation Group, IMCG: Internal Medicine Consultation Group, HAD: Hospital Anxiety and Depression scale

Table 3. Comparison of all groups in terms of somatosensory amplification						
Groups	**NCG (n=43)**	**GCG (n=48)**	**CCG (n=38)**	**IMCG (n=40)**	**Control (n=32)**	**Statistics**
SSAS (Mean ± SD)	27.74±6.30	32.31±6.94	28.42±6.76	28.90±6.17	8.59±2.21	F=82.893 p=0.000
NCG: Neurology Consultation Group, GCG: Gastroenterology Consultation Group, CCG: Cardiology Consultation Group, IMCG: Internal Medicine Consultation Group, HAD: Hospital Anxiety and Depression scale						

DISCUSSION

In our study, we found that the mean depression score of patients consulting from NCG, GCG, CCG, and IMCG was above the cut-off point of the test. In some patients, depression may present with pain, gastrointestinal disorders, and cardiac symptoms instead of vegetative symptoms. This condition is called masked depression in the literature (1). High rates of depression have been found in various patient groups in previous studies (1,7). In the study conducted by Korkmaz et al. (7), statistically higher rates of depression were found in cardiology patients with normal angiography compared to the control group. In our study, no difference was found between the consultation groups in terms of depression values. However, a difference was found between anxiety values. The difference was that the mean anxiety of the CCG was found to be higher than other groups. The literature indicates that anxiety is high in cardiologic patients. These results are compatible with our study (7,8). Symptoms such as palpitations, chest pain, and shortness of breath, which are the leading symptoms of panic disorder, overlap with cardiologic symptoms. In this case, psychological examination is important in diagnosing the disease (9).

In our study, all consultation groups had statistically significantly higher SSA values than the control group. This result is consistent with studies conducted with various patient groups (8,10). In our study, consultation groups were found to differ in SSA values. The difference was thought to be due to the high values of the GCG group. This factor is more prominent especially in patients presenting for a gastroenterology consultation. Studies have shown that patients who have IBS have higher levels of somatic amplification (11,12). In this study, although the patients with GCG did not have a gastroenterological diagnosis yet, their symptoms were similar, including abdominal pain, indigestion, diarrhea or constipation, and bloating.

Study Limitation

This study has several limitations. First, the sample size was relatively small, and the participants were recruited from only two centers, which may limit the generalizability of the findings. Second, the cross-sectional design prevents the establishment of causal relationships between physical symptoms and psychiatric outcomes. Third, although validated scales were used, reliance on self-reported questionnaires may have introduced response biases. Lastly, certain confounding variables such as socioeconomic status, chronic medical conditions, and medication use were not controlled, which might have influenced the results. Future studies with larger, multi-center samples and longitudinal designs are recommended to confirm and expand upon these findings.

CONCLUSION

In conclusion, this study demonstrated that patients referred to psychiatry outpatient clinics for consultation exhibited high levels of SSA, accompanied by elevated rates of depression and anxiety symptoms. These findings emphasize the importance of comprehensive psychiatric evaluation in patients presenting with unexplained physical complaints. Although the underlying mechanism of SSA, whether functional or structural in origin, remains unclear, further research is necessary to better understand its neurobiological basis and clinical implications.

Ethics

Ethics Committee Approval: The approval of the University of Health Sciences Türkiye, Adana City Training and Research Hospital Clinical Research Ethics Committee and was obtained (decision number: 191, date: 10.10.2024).

Informed Consent: Written informed consent was obtained from all participants, including those in the control group.

Footnotes

Authorship Contributions

Concept: E.Ç., Design: Y.Ö., B.K., Data Collection or Processing: Y.Ö., C.C., B.K., Analysis or Interpretation: E.Ç., B.K., Literature Search: Y.Ö., E.Ç., Writing: Y.Ö., E.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Aydemir Ö. Konsültasyonda psikiyatrik tanı. Psikiyatri Konsültasyonu El Kitabı. Matsan.1999
2. Barsky AJ, Wyshak G, Klerman GL. The somatosensory amplification scale and its relationship to hypochondriasis. J Psychiatr Res. 1990;24:323-34. doi: 1016/0022-3956(90)90004-a.
3. Perez DL, Barsky AJ, Vago DR, Baslet G, Silbersweig DA. A neural circuit framework for somatosensory amplification in somatoform disorders. J Neuropsychiatry Clin Neurosci. 2015 Winter;27(1):e40-50. doi: 10.1176/appi.neuropsych.13070170. Epub 2014 Nov 10.

4. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361-70. doi: 10.1111/j.1600-0447.1983.tb09716.x.
5. Aydemir Ö, Güvenir T, Küey L, Kültür S. Reliability and validity of the Turkish version of hospital anxiety and depression scale. Türk Psikiyatri Dergisi. 1997;8(4):280-7.
6. Güleç H, Sayar K. Reliability and validity of the Turkish form of the somatosensory amplification scale. Psychiatry Clin Neurosci. 2007;61:25-30. doi: 10.1111/j.1440-1819.2007.01606.x.
7. Korkmaz H, Korkmaz S, Yıldız S, Gündoğan B, Atmaca M. Determination of health anxiety, anxiety, and somatosensory amplification levels in individuals with normal coronary angiography. Biomed Res Int. 2017;2017:114-7. doi: 10.1016/j.psychres.2017.02.057.
8. Zincir SB, Sümbül M, Sümbül EA, Dalkılıç B, Cengiz F, Kıvrak T, et al. Evaluation of alexithymia, somatosensory sensitivity, and health anxiety levels in patients with noncardiac chest pain. Biomed Res Int. 2014;2014:1-6. doi: 10.1155/2014/896183.
9. Neill JR. Panic disorder and psychiatric consultation. Practical manual of psychiatric consultation. Baltimore: Williams & Wilkins. 1980.
10. Spano VE, Imbriglio TV, Ho KCJ, Chow JCF, Cioffi I. Increased somatosensory amplification is associated with decreased pressure pain thresholds at both trigeminal and extra-trigeminal locations in healthy individuals. J Oral Rehabil. 2021;48(1):10-17. doi: 10.1111/joor.13101. Epub 2020 Oct 7.
11. Tuğal Ö, Özenli Y, Cengisiz C, Topal K, Taşdoğan B, Karaköse S, et al. Is there any somatosensory amplification in patients with irritable bowel syndrome? Journal of Clinical and Analytical Medicine. 2017;8(suppl 4): 251-5. doi: 10.4328/JCAM.4937.
12. Özenli Y, Yoldaşcan E, Topal K. Özcürümez G. Prevalence and associated risk factors of somatization disorder among Turkish university students at an education faculty. Anatolian J Psychiatry. 2009; 10(2):131-6.

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Original Article

6

Radiological Findings in Pediatric Firearm Extremity Injuries

Pediatrik Ateşli Silah Ekstremite Yaralanmalarında Radyolojik Bulgular

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ABSTRACT

Objective: To evaluate the damage to soft tissue and bone, the presence of foreign bodies within the tissue, and associated injuries in firearm-related extremity injuries in children with different weapons, based on radiological findings.

Material and Methods: Patients who were admitted to the pediatric emergency department of University of Health Sciences Türkiye, Adana City Training and Research Hospital between January 1, 2018, and December 31, 2021, with firearm-related extremity injuries were included. Data on age, gender, weapon type, radiological examinations, hospitalization, intervention status, and clinical outcomes were collected. Radiological images were evaluated to determine soft tissue and bone damage, the presence of foreign bodies, and associated injuries.

Results: Among the 72 cases, 80% were male, with a median age of 164.6 months. Injuries were caused by shotguns in 51% and by handguns in 36%. Among those injured by handguns, 18 cases had isolated soft tissue injuries, 1 had vascular injury, and 7 had bone fractures. In six of the cases with isolated soft tissue injuries, the bullet core was surgically removed under local anesthesia. Five patients with bone fractures and one with vascular injury were hospitalized and underwent surgical treatment. Among those injured by shotguns, 33 cases had isolated soft tissue injuries, 2 sustained bone fractures, 1 sustained both a bone fracture and vascular injury, and 1 sustained nerve damage. All cases, except those with isolated soft tissue injuries, were hospitalized and received surgical treatment.

Conclusion: When a bullet core impacts bone, it tends to cause more severe damage compared to when it only passes through soft tissue. Bullet cores and shotgun pellets, that hit soft tissue can cause vascular injuries, and computed tomography angiography should be considered when vascular damage is suspected. Soft tissue injuries caused by bullet cores or buckshots can lead to nerve damage, making it essential to perform a thorough neurological examination of the injured extremity.

Keywords: Child, gunshot wounds, extremity, vascular injury, nerve damage

ÖZ

Amaç: Çocuklarda ateşli silahlar ile gerçekleşen ekstremite yaralanmalarında silah türüne göre farklılık gösteren yumuşak doku ve kemikte meydana gelen hasarı, dokuda yabancı cisim varlığını, eşlik eden yaralanmaları radyolojik bulgular eşliğinde incelemektir.

Gereç ve Yöntemler: Türkiye Sağlık Bilimleri Üniversitesi, Adana Şehir Eğitim ve Araştırma Hastanesi çocuk acil servisine 01.01.2018-31.12.2021 tarihleri arasında getirilmiş olan ve ateşli silahlar ile ekstremite yaralanması gerçekleşen olgular dahil edilmiştir. Olguların yaş, cinsiyet, silah çeşidi, radyolojik tetkikleri, hastaneye yatış, müdahale durumu ve klinik sonuçları kayıt edilmiştir. Radyolojik görüntüler yumuşak doku, kemik hasarı, dokuda yabancı cisim varlığı ve eşlik eden damar yaralanması açısından değerlendirilmiştir.

Bulgular: Çalışmaya dahil edilen 72 olgunun %80'i erkek, yaş median 164,6 (127-189) aydı. Yaralanma %51 tüfek, %36 tabanca aracılığı ile gerçekleşmişti. Tabanca ile yaralanan 18 olguda izole yumuşak doku yaralanması, 1 olguda damar yaralanması, 7 olguda kemikte kırık saptanmıştır. İzole yumuşak doku yaralanması olan 6 olguda mermi çekirdeği lokal anestezi eşliğinde cerrahi olarak çıkartılmıştır. Kemik kırığı saptanan 5 olgu ve damar yaralanması saptanan 1 olgu cerrahi olarak tedavi edilmiştir. Av tüfeği ile yaralanan 33 olguda izole yumuşak doku yaralanması, 2 olguda kemikte kırık, 1 olguda kemikte kırık ve damar yaralanması, 1 olguda sinir hasarı saptanmıştır. İzole yumuşak doku yaralanması dışındaki tüm olgular hastaneye yatırılarak cerrahi olarak tedavi edilmiştir.

Sonuç: Tüm olgulara uygun yöntemle X-ray grafi çekilmesi gerektiği, mermi çekirdeğinin kemiğe isabet etmesi durumunda sadece yumuşak dokudan geçen mermi çekirdeğine göre daha şiddetli hasar yaratacağı, yumuşak dokuya isabet eden mermi çekirdeği ve saçma tanelerinin damar yaralanmasına yol açabileceği, damar yaralanması düşünülen olgularda bilgisayarlı tomografi-anjiografi istenmesinin gerekli olduğu, aynı şekilde yumuşak dokuya isabet eden mermi çekirdeği ve saçma tanelerinin sinir hasarına neden olabileceği, yaralanan ekstemitenin ayrıntılı nörolojik muayenesinin yapılması gerektiği düşünülmektedir.

Anahtar Kelimeler: Çocuk, ateşli silah yaralanması, ekstremite, vasküler yaralanma, sinir hasarı

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INTRODUCTION

Every day, an increasing number of children are injured or killed by firearms, due to factors such as the ease of obtaining weapons, inadequate security measures during possession, negligence, and lack of education. While the extremities are the most frequently affected areas in firearm injuries (FI), the mortality rate in these cases is lower than in injuries to the head, neck, chest, and other critical regions (1-3).

Essentially, injury results from energy transfer, which depends on the ability of the bullet core or buckshot to transfer energy to the tissue. Deformation develops in the bullet core when a 9 × 19 mm handgun, a low energy weapon commonly used, strikes bone tissue. Deformation refers to the change in shape and contours of the bullet core upon impacting a hard surface. In such instances, the increased energy of the bullet core is transferred more rapidly to the surrounding tissue via the friction surface. When a bullet core hits thick bones such as the pelvis, vertebrae, femur, or humerus, the resulting fragmentation of the bullet core is referred to as primary fragmentation, while the fracturing and fragmentation of the bone itself is termed secondary fragmentation. The significance of fragmentation lies in the fact that each fragment behaves like a bullet core, increasing the extent of damage by transferring energy to the surrounding tissues, thereby further exacerbating tissue damage (4-8). Injuries caused by shotgun buckshots exhibit different characteristics from those caused by handgun bullet cores. Buckshots, fired in a cluster from a shotgun, disperse based on the shooting distance, transfer kinetic energy to the tissue, and cause tissue damage (9-11).

Based on radiological findings, the aim of this study was to evaluate the damage to soft tissue and bone, the presence of foreign bodies within the tissue, and associated injuries in firearm-related extremity injuries in children.

MATERIALS and METHODS

This cross-sectional study was conducted on patients who were admitted to the pediatric emergency department of the tertiary Adana Training and Research Hospital between January 1, 2018, and December 31, 2021, with firearm-related extremity injuries. Data on age, gender, weapon type, radiological examinations [(X-ray and/or tomography and computed tomography (CT) angiography)], hospitalization, intervention status (medical or surgery), and clinical outcomes (death or discharged) were collected. Radiological images from the hospital information management system were independently evaluated by two researchers, who were blinded to each other's assessments, to determine soft tissue and bone damage, the presence of foreign bodies, and associated injuries.

Ethical approval for the study was obtained from the Clinical Research Ethics Committee of University of Health Sciences Türkiye, Adana City Training and Research Hospital on March 14, 2024 (decision no: 3223).

Statistical Analysis

The Statistical Package for Social Sciences (SPSS 21.0; Chicago, IL) was used for data analysis. Continuous variables were expressed as the median (interquartile range: 25-75), while categorical variables were expressed as the number and percentages. A cross-tabulation was generated to examine the distribution of two different categorical variables.

RESULTS

Among the 72 cases included in the study, 80% (58/72) were male, and the median age was 164.6 (127-189) months. The injury location was the lower extremity in 67% (48/72), the upper extremity in 22% (16/72), and both upper and lower extremities in 11% (8/72). The most frequent consultations were requested from the orthopedics and cardiovascular surgery departments. Injuries were caused by shotguns in 51% (37/72) and by handguns in 36% (26/72). No information about the weapon type could be obtained for 9 cases; these patients were treated as outpatients, and no foreign body was detected in their radiographs (Table 1).

Of the 26 cases injured by handguns, 18 had isolated soft tissue injuries, 1 had vascular injury, and 7 had bone fractures. In 6 of the cases with isolated soft tissue injuries, the bullet core was surgically removed under local anesthesia. Five cases with bone fractures and 1 with vascular injury were hospitalized and underwent surgical treatment. Of the 37 cases injured by shotguns, 33 had isolated soft tissue injuries, 2 had bone fractures, 1 had both bone fracture and vascular injury, and 1 had nerve damage. All cases, except those with isolated soft tissue injuries, were hospitalized and received surgical treatment. There were no fatalities among the cases included in this study.

Bullet cores, and their related soft tissue deformation, bone fractures and vascular damage resulting from handgun injuries are shown in Figures 1-3. Buckshots and their related soft tissue deformation and bone fractures resulting from shotgun injuries are shown in Figures 4-6.

Table 1. Patients' demographic and injury findings according to weapon type				
	Total (n: 72)	**Shotgun (n: 37)**	**Handgun (n: 26)**	**Unknown (n: 9)**
Age	164.6 (127-189)	180 (157-192)	191 (158-204)	122 (69-174)
Gender				
Female	14 (19.6%)	7 (9.8%)	4 (5.6%)	3 (4.2%)
Male	58 (80.4%)	30 (41.5%)	22 (30.5%)	6 (8.4%)
Injury location				
Upper extremity	48 (66.4%)	18 (25%)	23 (31.6%)	7 (9.8%)
Lower extremity	16 (22.4%)	11 (15.4%)	3 (4.2%)	2 (2.8%)
Upper + lower extremity	8 (11.2%)	8 (11.2%)	-	-
Injured tissue				
Isolated soft tissue injury	60 (83.2%)	33 (45.6%)	18 (25%)	9 (12.6%)
Bone fracture	9 (12.6%)	2 (2.8%)	7 (9.8%)	-
Vascular injury	1 (1.4%)	-	1 (1.4%)	-
Nerve injury	1 (1.4%)	1 (1.4%)	-	-
Bone fracture + vascular injury	1 (1.4%)	1 (1.4%)	-	-
Treatment				
Medical	56 (77.8%)	33 (45.8%)	14 (19.4%)	9 (12.6%)
Surgery	16 (22.2%)	4 (4.2%)	12 (18%)	-

DISCUSSION

In our study, similar to findings in the literature, 80% of the cases were male and the median age was 164.6 months. Although the weapon type is influenced by factors such as geographical region and social and cultural differences, research in Türkiye, has shown that firearm related injuries and fatalities are more common than those caused by handguns. For instance, the weapon distribution was reported as 66% shotgun and 34% handgun in Konya; 65.8% shotgun and 34.2% handgun in İzmir; 59.4% shotgun and 40.6% handgun in Muğla; 65.8% shotgun and 34.2% handgun in Manisa, and 51% shotgun and 36% handgun in our study. The higher frequency of firearm-related injuries and deaths is attributed to their easy availability and widespread presence in homes, often stored unsafely, especially in rural areas where agriculture and animal husbandry are common (12-18).

In cases involving handguns, isolated soft tissue injuries were observed in 18 cases, vascular injury in 1 case, and bone fractures in 7 cases. In 6 cases with isolated soft tissue injuries, the bullet core was surgically removed using local anesthesia. Five cases with bone fractures and one with vascular injury required hospitalization and surgical treatment. According to our findings, cases with isolated soft tissue injuries caused by low energy weapons that do not involve vascular, nerve, or bone damage can be managed on an outpatient basis. However, when the bullet core impacts bone and causes fragmentation due to deformation, surgical treatment may be necessary. Cases with vascular injuries must be hospitalized and treated surgically.

In shotgun injuries, buckshot enter the body in clusters and disperses depending on the shooting distance, causing damage by transferring energy to the affected tissues. At close range, shotgun injuries can cause more severe damage than handgun injuries (7,11). In our study, 33 cases had isolated soft tissue injuries, 2 cases had bone fractures, 1 case had both a bone fracture and vascular damage, and 1 case had nerve damage. All cases, except those with isolated soft tissue injuries, were hospitalized and treated surgically. In one case, where an injury to the left arm was sustained, the buckshot caused significant tissue loss and ulnar nerve damage. Our findings indicate that shotguns are associated with fewer bone fractures but more vascular and nerve damage compared to handguns. Therefore, except for cases with isolated soft tissue injuries, surgical treatment, and hospitalization should be considered.

Although the severity of FI depends on the type of weapon and the area hit, extremity injuries can affect peripheral vessels, nerves, and the spinal cord, in addition to bones and soft tissues. It is important to remember that even small entry wounds may be accompanied by serious internal bleeding, a risk of compartment syndrome, and damage to major vessels as the bullet travels through the body. It is recommended that X-rays be taken after initial treatment and stabilization, ensuring that images are bidirectional and include both the proximal and distal parts of the injury site. X-rays should be evaluated for bullet core residue, fragmented bullet cores, bone fractures, displaced bone fragments, and soft tissue injuries. Air densities in areas outside the injury zone could indicate cavitation (19,20).

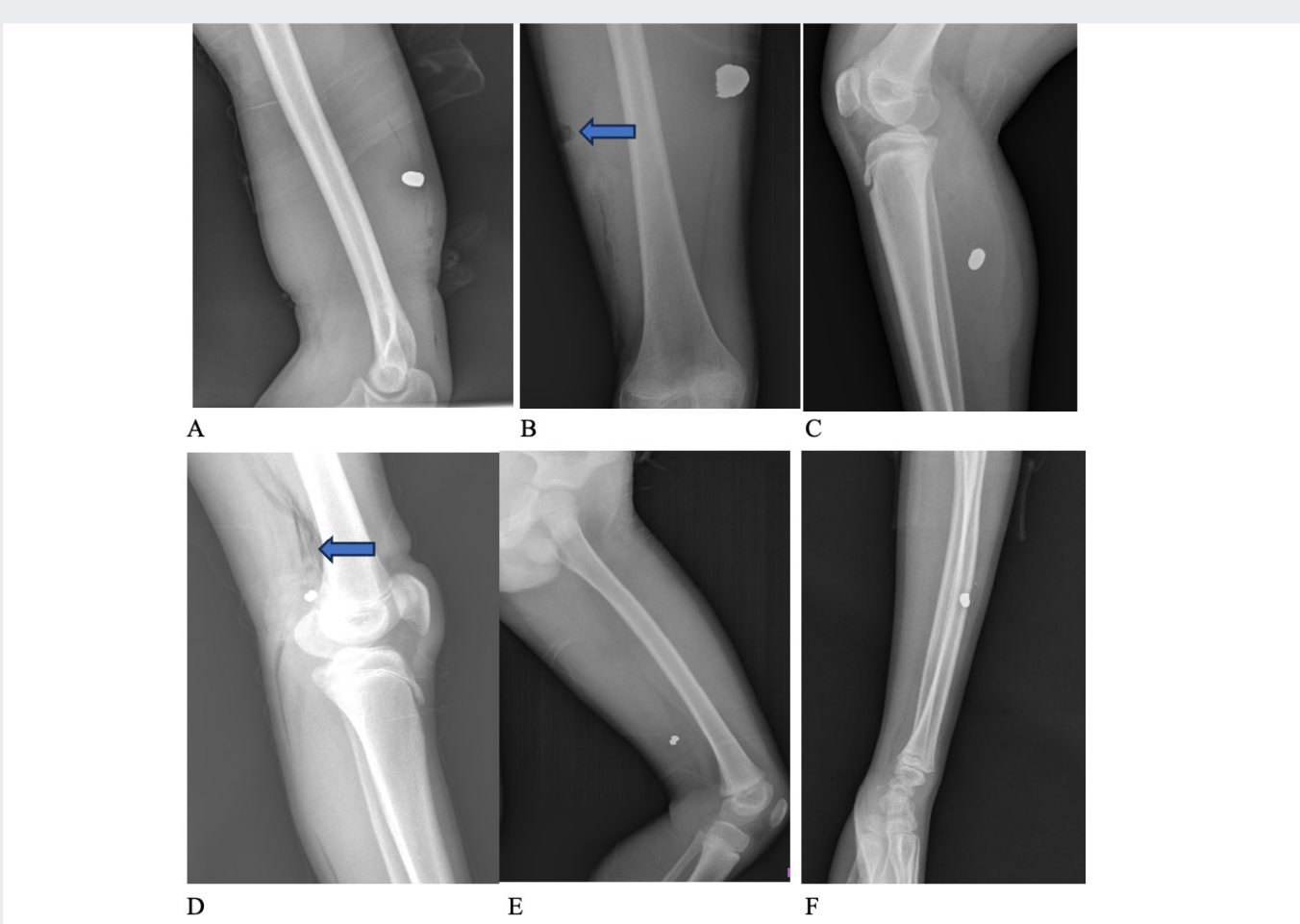

Figure 1. Isolated soft tissue injury with handgun (A) Bullet core lodged in soft tissue of right arm. (B) Bullet core and entry wound in soft tissue of right thigh (blue arrow) (C) Bullet core in soft tissue of left leg (D) Bullet core and cavitation in the soft tissue behind the left knee (blue arrow) (E) Bullet core in the soft tissue of the left distal thigh (F) Bullet core in soft tissue of left forearm

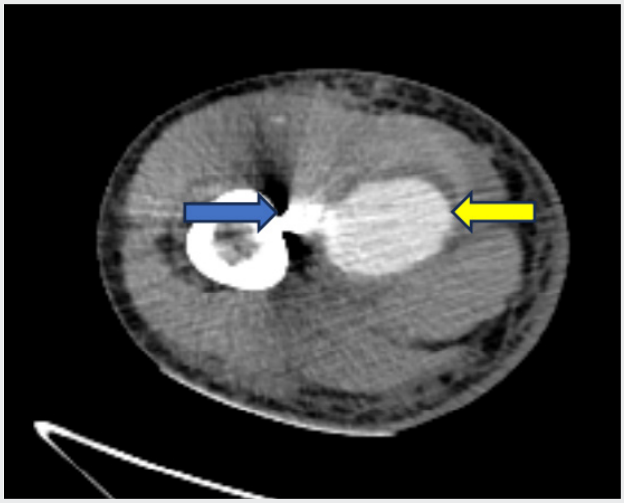

Figure 2. Handgun injury, bullet core (blue arrow) and vascular injury (yellow arrow) in soft tissue

In children, FI is one of the most common causes of vascular damage. Even if a blood vessel supplying an organ is not directly hit, it may be injured if it is within the temporary cavity created by the bullet. While the media and adventitia layers of the vessel are composed of strong elastic fibers and can withstand sudden stretching and compression, the single-layer epithelial structure of the intima may tear, leading to coagulation and subsequent clot formation, which can result in necrosis in the affected organ. Signs of vascular injury include abnormal pulse in the injured extremity, expanding hematomas, pulsatile bleeding, entry and exit wounds near vascular regions, and abnormal vascular Doppler examination findings. Mortality is higher in cases of suspected vascular damage in firearm-related extremity injuries, making it crucial to perform CT angiography promptly and plan appropriate surgical intervention (21-23). In our study, CT angiography was performed on 20 cases, with vascular damage detected in 4 of them. These cases were admitted to the cardiovascular surgery department and underwent surgical intervention.

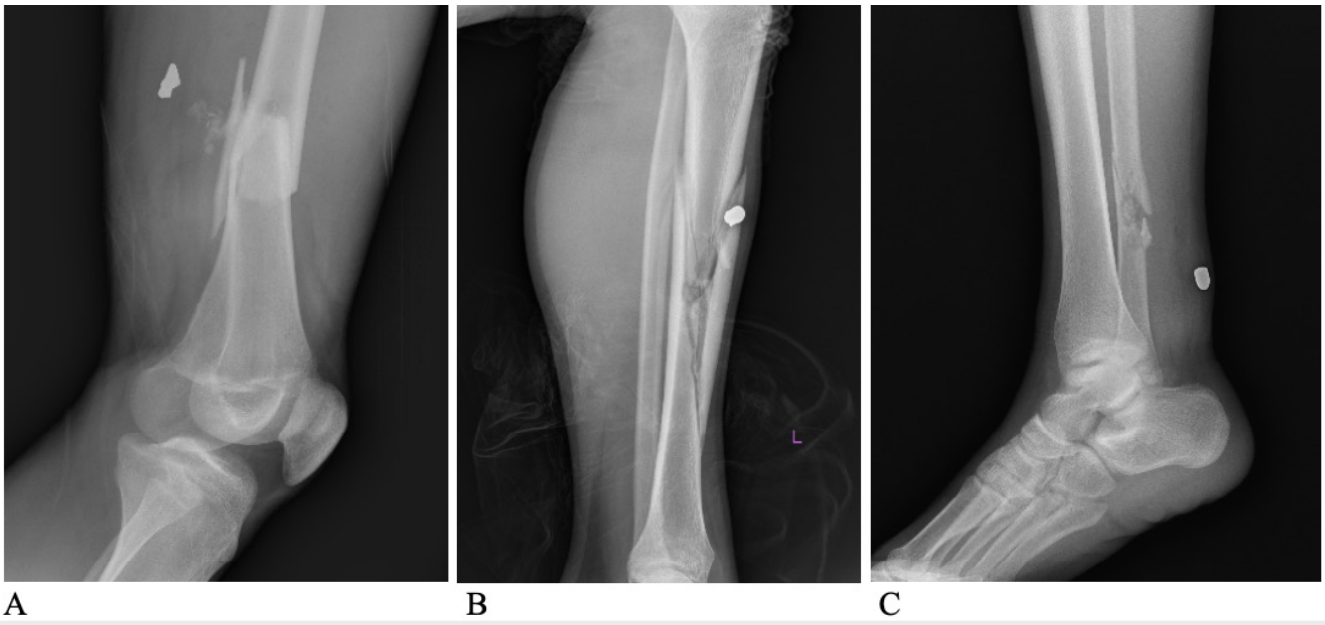

Figure 3. Handgun injury (A) Left distal femur fracture and soft tissue deformation (B) Left tibial shaft fracture and bullet core in the bone (C) Right distal tibia fracture and bullet core in soft tissue

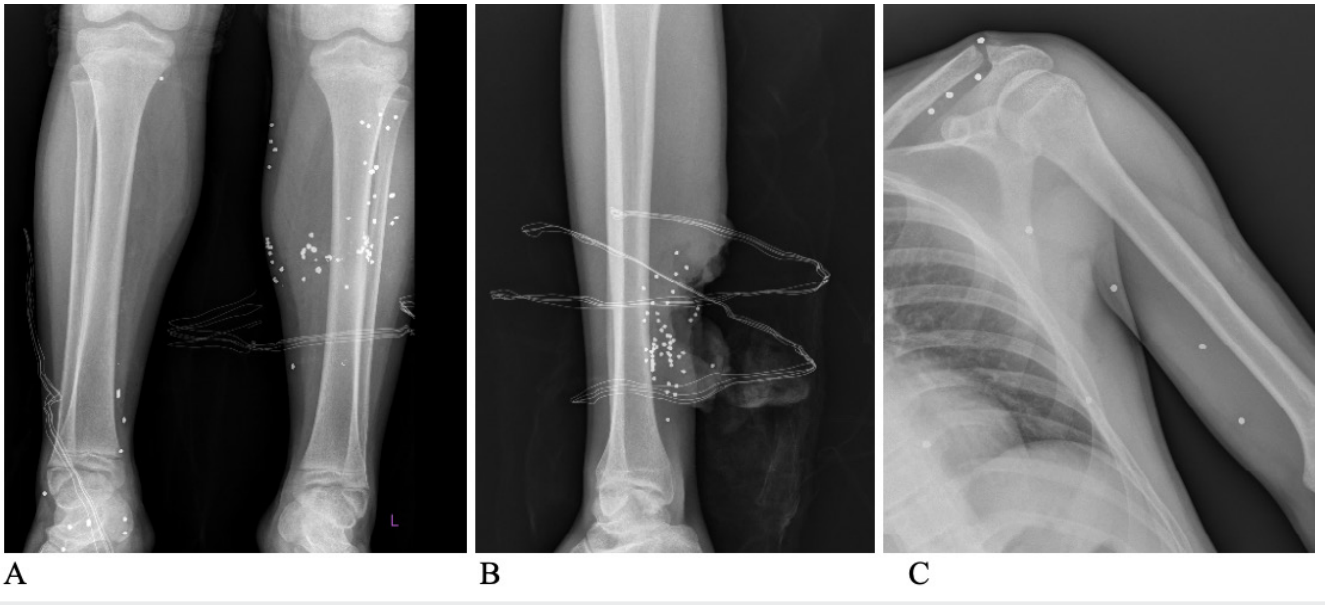

Figure 4. Shotgun injury (A) Soft tissue buckshots in bilateral lower extremities (B) Soft tissue injury and buckshots in the distal right leg (C) Buckshots in soft tissue of left arm and shoulder

Neurological damage is more common in the upper extremity and its associated with morbidity, chronic pain and disfunction (24,25) In one case involving a shotgun injury, extensive tissue damage and ulnar nerve injury were identified, and the patient was hospitalized under the care of the orthopedics department, where surgical intervention was performed.

Study Limitation

A limitation of this study is its retrospective design, which resulted in incomplete information regarding the type of weapon used, the circumstances of the incident, and the shooting distance. However, since the primary objective of the study was to assess injury through radiological findings, we

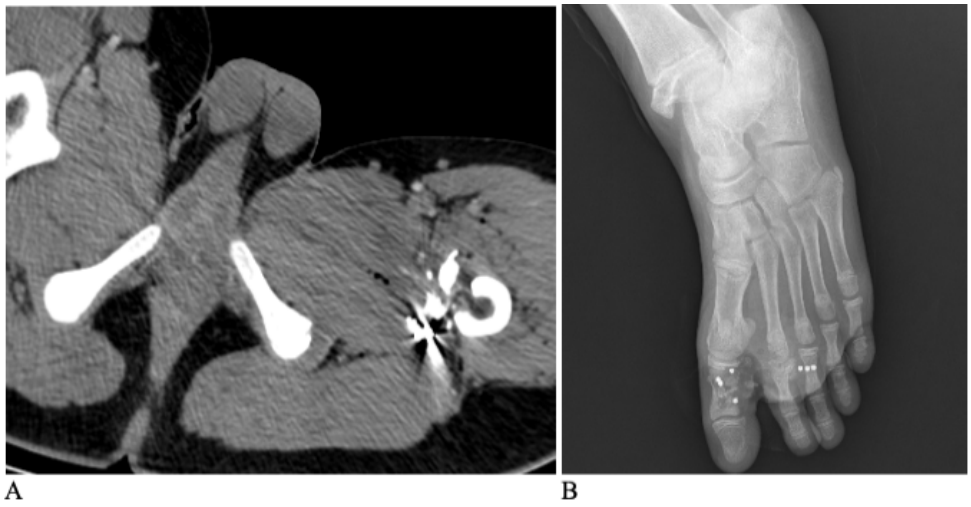

Figure 5. Shotgun injury (A) Fracture and buckshot in the proximal left femur (B) Fractures and buckshots in the right foot

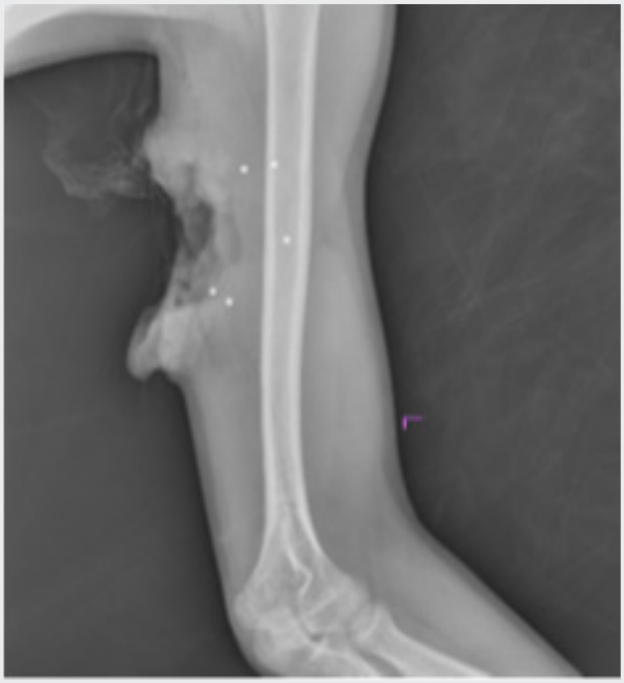

Figure 6. Shotgun injury, soft tissue injury to left arm and buckshots

believe that these historical gaps do not significantly impact the study's results.

CONCLUSION

Although FI encountered in civilian settings typically involves lower energy weapons than those seen in military environments, they can still cause significant trauma and damage. Understanding the structural differences between bullet cores and shotgun pellets, as well as the kinetic energy at the moment of impact, is essential to guiding treatment approaches. Knowledge of weapon mechanisms and their wounding potential is crucial.

According to our study, when a bullet core impacts bone, it tends to cause more severe damage compared with when it only passes through soft tissue. Additionally, bullet cores and shotgun pellets that hit soft tissue can cause vascular injuries, and CT angiography should be considered when vascular damage is suspected. Similarly, soft tissue injuries caused by bullet cores or buckshots can lead to nerve damage, making it essential to perform a thorough neurological examination of the injured extremity.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Clinical Research Ethics Committee of University of Health Sciences Türkiye, Adana City Training and Research Hospital on March 14, 2024 (decision no: 3223).

Informed Consent: This cross-sectional study was conducted on patients who were admitted to the pediatric emergency department of the tertiary Adana Training and Research Hospital between January 1, 2018, and December 31, 2021, with firearm-related extremity injuries.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.S.K., İ.A., Concept: A.S.K., İ.A., Design: A.Y., A.S.K., İ.A., Data Collection or Processing: A.Y., A.S.K., İ.A., Analysis or Interpretation: A.Y., İ.A., Literature Search: İ.A., Writing: A.Y., S.B., A.S.K., İ.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Çınar T, Alkan N, Büyük Y. Gunshot cases evaluated by the first specialization committee and the department of ballistics of the Institute of Forensic Medicine, Ministry of Justice. Tıp Fak Mecmuası. 2002;65(1):47-52.
2. Aydın F, Yavuz MS. Childhood deaths due to firearm injuries in İzmir and Nearby Cities. The Bulletin of Legal Medicine. 2020;25(1):36-43.
3. Can M, Çakar A, Gözen A, Türközü T. Gunshot injuries in children treated in the department of orthopedics. Balıkesir Health Sciences Journal. 2012;1(3):97-102.
4. Öğünç Gİ, Kaymak Ş, Uzar Aİ. Ateşli silah yaralanmalarının özellikleri ve balistik bilimi. Türkiye Klinikleri. 2020;1:1-7.
5. Uzar Aİ, Güleç B, Kayahan C, Özer MT, Öner K, Alpaslan F. Wound ballistics- ı effects of permanent and temporary wound cavities. Ulusal Travma Derg. 1998;4(4):225-9.
6. Arslan İ. Ateşli Silah yaralanmalarında hemodinamik ve histolojik bulgular. Çukurova Üniversitesi bağımlılık ve Adli Bilimler Enstitüsü, Adli Bilimler Anabilimdalı. Doktora Tezi. 2014.
7. Uzar Aİ, Öğünç Gİ, Özer MT. Wound ballistics in penetrating gunshot injuries. Güvenlik Bilimleri Dergisi. 2019;özel sayı:53-77.
8. Özer MT. Wound ballistic of gunshot injuries with high kinetic energy and reflections to the surgical treatment. Okmeydanı Tıp Derg. 2017;33(1):40-7.
9. Uzar Aİ, Dakak M, Öner K, Ateşalp AS, Yiğit T, Özer T, et al. Comparison of soft tissue and bone injuries caused by handgun or rifle bullets: an experimental study. Acta Orthop Traumatol Turc. 2003;37(3):261-7.
10. Çelikel A, Balcı Y, Üner B, Bal C. The effect of barrel lenght an pallet dispersion and its importance in determeination of fire. J For Med. 2012;26(2):115-23. doi: 10.5505/adlitip.2012.84803.
11. Koç S, Şam B, Yılmaz R. Av tüfeği yaralanmalarının adli tıbbi boyutu. Acta Turcica Çevrimiçi Tematik Türkoloji Dergisi. 2009;1(1):213-27.
12. Demirci Ş, Doğan KH, Deniz İ, Büken B, Erkol Z. The deaths related to firearm injuries during the age of childhood in Konya. Adli Tıp Bülteni. 2009;14(1):22-9.
13. Aydın F, Yavuz MS. Childhood deaths due to firearm injuries in ızmir and nearby cities. Adli Tıp Bülteni, 2020;25:36-43.
14. Aydn F. Ateşli silah yaralanmasına bağlı 18 yaş altı ölümler. Manisa Celal Bayar Üniversitesi Tıp Fakültesi Adli Tıp Anabilim Dalı. Uzmanlık Tezi. 2019.
15. Ekinci E, Balcı Y, Çallak F, Anolay N. Demographic characteristics and autopsy findings by origin of deaths due to firearm ınjury-analytical research. Adli Tıp Bülteni. 2023;28(1):15-22.
16. Turgut K, Gür A, Güven T, Oğuztürk H. Evaluation of factors related to mortality caused by firearm injury: a retrospective analysis from Malatya, Turkey. Arch Iran Med. 2019;22(2):80-4.
17. Kodik MS, Akdöner ÖB, Özek ZC. An evaluation of firearm injuries in the emergency department. Cureus. 2021;13(12):20555. doi: 10.7759/cureus.20555.
18. Çaylak H, Genç O. Toraksı ilgilendiren ateşli silah yaralanmaları. Toraks Cerrahisi Bülteni, 2010;1:29-32.
19. Kim PE, Go JL, Zee CS. Radiographic assessment of cranial gunshot wounds. Neuroimaging Clin n Am. 2002;12(2):229-48. doi: 10.1016/s1052-5149(02)00007-2.
20. Karaca MA, Kartal ND, Erbil B, Öztürk E, Kunt MM, Şahin TT, et al. Evaluation of gunshot wounds in the emergency department. Ulus Travma Acil Cerrahi Derg. 2015;21(4):248-55. doi: 10.5505/tjtes.2015.64495.
21. Jigarkumar AP, White JM, White PW, Rich NM, Rasmussen TE. A contemporary, 7 year analysis of vascular injury from the war in Afghanistan. J Vasc Surg. 2018;68(6);1872-9. doi: 10.1016/j.jvs.2018.04.038.
22. Gakdal MS, Sartip KA. CT angiography signs of lower extremity vascular trauma. AJR. 2009;193:49-57. doi: 10.2214/AJR.08.2011.
23. Gopireddy DR, Kee-Sampson JW, Vulasala SSR, Stein R, Kumar S, Virarkar M. Imaging of penetrating vascular trauma of the body and extremities secondary to ballistic and stab wounds. J Clin Imaging Sci. 2023;13:1. doi: 10.25259/JCIS_99_2022.
24. Shields LBE, Iyer VG, Zhang YP, Shields CB. Gunshot-related nerve injuries of the upper extremities: clinical, electromyographic, and ultrasound features in 22 patients. Front. Neurol. 2024;14:1333763. doi: 10.3389/fneur.2023.1333763.
25. Chi D, Tandon D, Evans AG, Brown DJ, Payne RM, Van Handel AC, et al. Brachial gunshot wounds: injury patterns and considerations for managing the abnormal neurological examination. Hand(NY). 2025;19:15589447231221170. doi: 10.1177/15589447231221170.

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Original Article

13

Electrophysiologic and Histopathological Evaluation the Fibrinolytic Effect of Streptokinase in Experimental Hematomyelia

Deneysel Hematomyelide Streptokinazın Fibrinolitik Etkisinin Elektrofizyolojik ve Histopatolojik Olarak Değerlendirilmesi

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ABSTRACT

Objective: This study aimed to evaluate the local effects of streptokinase (SK) through histopathological analysis and electrophysiological assessment using somatosensory evoked pathway (SEP) measurements.

Material and Methods: A total of 54 male albino rabbits were used in this study. The rabbits were categorized into three groups: 6 for the standardization group; 24 for the experimental group, and 24 for the control group. Following the induction of experimental hematomyelia in both the control and experimental groups, SEP recordings were obtained on days 1, 3, 7, and 14. Frozen sections were also prepared for analysis.

Results: Findings indicated that recovery began on the third day in both the control and experimental groups, with SEP values being comparable. By the seventh day, improvement continued progressively in both groups, and SEP recordings remained similar. After 14 days, the greatest degree of recovery was observed in both groups, with SEP values approaching those of the standardization group.

Conclusion: This experimental study demonstrated that there was no therapeutic benefit when performing histopathologic evaluation and statistical analysis of electrophysiological amplitude and latency values. Therefore, local administration of SK was found to be ineffective in the treatment of hematomyelia.

Keywords: Streptokinase, hematomyelia, spinal local effects

ÖZ

Giriş: Bu çalışmanın amacı streptokinazın (SK) lokal etkilerini histopatolojik analiz ve somatosensoriyel uyarılmış yol (SEP) ölçümleri kullanılarak elektrofizyolojik değerlendirme yoluyla değerlendirmektir.

Gereç ve Yöntemler: Bu çalışmada toplam 54 erkek albino tavşan kullanıldı. Tavşanlar standardizasyon için 6, deney grubu için 24 ve kontrol grubu için 24 olmak üzere üç gruba ayrıldı. Hem kontrol hem de deney gruplarında deneysel hematomiyeli indüksiyonunu takiben 1, 3, 7 ve 14. günlerde SEP kayıtları alındı. Analiz için don kesitleri de hazırlandı.

Bulgular: Bulgular hem kontrol hem de deney gruplarında iyileşmenin üçüncü günde başladığını ve SEP değerlerinin karşılaştırılabilir olduğunu gösterdi. Yedinci güne kadar, iyileşme her iki grupta da aşamalı olarak devam etti ve SEP kayıtları benzer kaldı. On dört gün sonra, her iki grupta da en yüksek derecede iyileşme gözlendi ve SEP değerleri standardizasyon grubununkilere yaklaştı.

Sonuç: Bu deneysel çalışma, histopatolojik değerlendirmenin ve elektrofizyolojik amplitüd ve latans değerlerinin istatistiksel analizinin terapötik bir fayda sağlamadığını göstermiştir. Bu nedenle, SK'nin lokal uygulamasının hematomyeli tedavisinde etkisiz olduğu bulunmuştur.

Anahtar Kelimeler: Streptokinaz, hematomiyeli, spinal lokal etkiler

INTRODUCTION

Neurosurgeons frequently encounter traumatic or spontaneous hemorrhages of the central nervous system, particularly in treatment applications. While advancements in diagnostic and imaging techniques have enabled rapid and precise identification of various neural pathologies, ongoing research aims to develop effective treatment protocols for conditions such as cerebral edema, spinal contusion, vasospasm, cerebral hemorrhages, hematomyelia.

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The primary mechanism in hematoma resolution is the activation of the fibrinolytic system. The compartments of the central nervous system, the brain enclosed by the cranium the spinal cord within the vertebral column, are anatomically similar due to their continuity and histologically identical neural elements. Studies on the fibrinolytic activity (FA) of brain tissue and its compartments have determined that, despite increased thromboblastic activation in brain tissue, FA is weak, while the meninges and choroid plexuses exhibit high activity. Studies on intracerebral hematomas have explored the use of streptokinase (SK), a fibrinolytic agent, demonstrating its efficacy by incorporating it into treatment protocols (1). However, no studies have evaluated the effects of fibrinolytic agents on hematomyelia. Hematomyelia can result in complete or partial lesions of the spinal cord, leading to motor and sensory deficits as well as autonomic dysfunctions such as sphincter impairment. It is recognized that comparing early electrophysiological recordings with clinical findings is valuable for evaluating the prognosis of neurological deficits following hematomyelia.

In this study, experimental hematomyelia was induced to examine the local effects of SK through histopathological analysis and electrophysiological assessment using somatosensory evoked potential measurements. Changes were evaluated over specific time intervals.

MATERIALS and METHODS

A total of 54 male albino rabbits, each weighing between 2500 and 3000 g, were used in the study. Electrophysiological assessments were conducted using a Medelec–Teca Premiere Plus EMG device. Anesthesia was induced with ketamine hydrochloride, a dissociative anesthetic.

SK was administered as a thrombolytic agent in the experimental groups. All rabbits were fasted 6 h prior to the procedure. For prophylactic purposes, ceftriaxone was administered intramuscularly at a dose of 50 mg/kg. Just before the experiment, anesthesia was induced with an intramuscular injection of 60 mg/kg ketamine hydrochloride. The rabbits were positioned prone on the operating table with their extremities and tails secured. The thoracic region and the upper lateral aspects of the right knee were shaved and disinfected with 10% povidone-iodine. A midline vertical incision, approximately 6-7 cm in length, was made in the upper thoracic region. The skin, subcutaneous fascia, and muscle layers were separated using blunt dissection. Laminectomy was performed at the T1-T4 levels to expose the spinal cord.

In the standardization group, somatosensory evoked pathway (SEP) recordings were obtained from six rabbits using a REM Medelec-Teca Premiere Plus EMG device. The recording parameters included a low filter of 20 Hz, a high filter of 10 kHz, a scan time of 10 msec, a sensitivity of 10 microvolts, a stimulation intensity of 12 milliamps, and a repetition rate of 2 pps. One electrode was placed subdurally at the T2 spinal segment, while the reference electrode was positioned on the adjacent muscle tissue. Dorsal column spinal cord potentials, consisting of a positive wave measuring 7.9±1.15 microvolts followed by 4 or 5 negative waves, were recorded 5.5±0.5 msec after stimulation.

The remaining 48 rabbits were assigned to control and experimental groups. Hematomyelia was induced in these rabbits by collecting 0.1 mL of autologous blood from the femoral artery using an insulin syringe, and injecting it intraspinally at a depth of 2 mm from the dura at the T4 segment with the aid of a guiding frame.

Among the rabbits with hematomyelia, the experimental group received 10,000 U/0.1 mL of SK, while the control group was administered 0.1 ml of saline. Both groups were further divided into four subgroups, each consisting of six rabbits. SEP recordings were performed on days 1, 3, 7, and 14. At the end of the follow-up period, the rabbits were euthanized using a high dose of the same anesthetic. The affected spinal cord segment was promptly extracted and fixed in 10% formalin. The tissues samples were then dehydrated in graded alcohol concentrations, cleared in xylene, embedded in paraffin, and section into blocks. For light microscopic examination, 3–5 micron-thick sections were prepared using a microtome, stained with hemotoxylin and eosin, and analyzed under an Olympus BX-50 1 light microscope in the Department of Pathology.

Magnetic resonance imaging (MRI) is specific and sensitive in the radiological diagnosis of hematomyelia. A Siemens Healthineers Magnetom Sola 1.5T was used as an MRI device. In the subject who underwent hematomyelia, the lesion appears hyperintense in the sagittal and axial planes at the T4 level on the T1 sequence MRI.

Histopathological grading was determined as grade 0 for a bleeding area of less than 5% at 40x magnification, grade 1 for 5-25%, grade 2 for 25-50%, and grade 3 for 50% or more.

Statistical Analysis

The electrophysiological results were statistically analyzed using the Student's t-test. Data obtained at the end of the study were evaluated according to this method. A p value of >0.05 was considered not statistically significant, while a p value of <0.05 was considered significant.

RESULTS

There were 6 rabbits in the standardization group. SEP recordings were performed at T2. Table 1 presents information on amplitude and latency values.

SEP measurements performed at the T2 spinal segment level in the dorsal cord 1 day after hematomyelia + saline fluid did not yield measurable amplitude or latency values for tractus functions.

There were 24 rabbits in the control group. SEP recordings were taken on the 3rd, 7th, and 14th day after hematomyelia.

Table 2 presents information on amplitude and latency values.

Similarly, SEP measurements at the T2 spinal segment level 1 day after hematomyelia + SK did not show any measurable tract function values. The observed SEP potential damage was identical in both the control and experimental groups after 1 day.

There were 24 rabbits in the experimental group. SEP recordings were taken on the 3rd, 7th, and 14th day after hematomyelia. Table 3 presents information on amplitude and latency values.

In both the control and experimental groups, improvement was observed starting on the third day, with recorded SEP values being similar between the groups. By the seventh day, the improvement continued progressively, and SEP values remained comparable. After 14 days, the highest level of recovery was recorded in both groups, with SEP values approaching those of the standardization group

In both the control and experimental groups, erythrocyte density, edema, inflammatory cell infiltration, and astrogliotic cell proliferation were assessed using a four-grade scale:

Table 1. Amplitude and latency values of the first positive wave in the standardization group (n=6)

Subject	1	2	3	4	5	6	X ± SD (n=6)
Amplitude (μV)	8.7	7.5	6.3	8.7	7.5	8.7	7.9±1.15
Latency (ms)	5.7	5.7	5.1	6.0	5.1	5.4	5.5±0.5

μV: Microvolt, ms: Milliseconds, SD: Standard deviation

Grade O: None

Grade 1: Mild

Grade 2: Moderate

Grade 3: Intense

Histopathologic results of the control group were obtained on the 1st, 3rd, 7th, and 14th days. Results over 4 grades are shown in table 4

Histopathologic results of the experimental group were obtained on the the 1st, 3rd, 7th, and 14th days. Results over 4 grades are shown in table 5.

DISCUSSION

Spinal cord injury results in the loss of supraspinal control of sensory, autonomic, and motor functions below the lesion level (2). This functional loss occurs suddenly and is irreversible following traumatic spinal cord injury, with secondary lesions developing due to a reactionary cascade. To facilitate the assessment of recovery of spinal cord injury in our model, we determined through histopathological examination that 1 μL of blood was sufficient to induce a neurological deficit in rats weighing approximately 250 g.

MRI has significantly improved the evaluation of various spinal pathologies and remains the primary radiologic diagnostic method for evaluating hematomyelia (2,3). In our study, we experimentally induced hematomyelia and confirmed hematoma formation using MRI. A total of 0.1 cc of autologous blood, collected from the femoral artery, was injected at a depth of 2 mm from the dura mater into the

Table 2. Amplitude and latency values of the first positive wave in the control group at 3, 7, and 14 days after hematomyelia

	Subject	1	2	3	4	5	6	X ± SD (n=6)
Day 3	Amplitude (μV)	2.5	2.5	3.7	2.5	2.5	2.5	2.37±0.327
	Latency (ms)	6.2	6.1	6.3	5.7	6.0	5.7	6.37±0.225
Day 7	Amplitude (μV)	2.5	2.5	3.7	2.5	2.5	2.5	2.7±0.490
	Latency (ms)	6.2	6.1	6.3	5.7	6.0	5.7	6.0±0.234
Day 14	Amplitude (μV)	9.0	6.2	6.9	6.9	7.5	6.2	7.2±1.886
	Latency (ms)	5.6	5.5	5.7	5.9	5.1	5.8	5.6±0.297

μV: Microvolt, ms: Milliseconds, SD: Standard deviation

Table 3. Amplitude and latency values of the first positive wave in the experimental group at 3, 7, and 14 days after hematomyelia + SK

	Subject	1	2	3	4	5	6	X ± SD (n=6)
Day 3	Amplitude (μV)	2.6	2.5	2.6	2.5	2.5	2.8	2.68±0.445
	Latency (ms)	6.3	6.1	6.2	6.5	6.6	6.3	6.24±0.234
Day 7	Amplitude (μV)	2.5	2.5	3.2	2.6	2.5	3.6	3.0±0.441
	Latency (ms)	6.1	6.2	5.8	5.7	6.0	5.9	5.87±0.187
Day 14	Amplitude (μV)	8.9	11.3	6.2	7.5	6.9	6.9	8.7±1.876
	Latency (ms)	5.5	5.4	5.7	5.9	5.2	5.8	5.52±0.264

μV: Microvolt, ms: Milliseconds, SD: Standard deviation, SK: Streptokinase

dorsal funiculus at the T4 spinal segment, using a guiding frame. Histopathological analysis revealed that this amount of blood was sufficient to induce a neurological deficit.

Previous studies have examined hematomyelia induction using different volumes. Fehlings al. (4) reported that 1 µL of hemorrhage in the human brain was equivalent to 0.75 mL in rats weighing approximately 250 g. Similarly, Milhorat et al. (2) used 2 µL of donor blood to experimentally induce hematomyelia in the dorsal funiculus of the spinal cord in rats. Given the morphological differences in spinal cord structure, weight, and volume between rats and rabbits, we aimed to create hematomyelia using 10 µL of autologous blood in our model.

In our experimental study, we found that SK increases FA, although it is possible to delay the improvement due to its toxic effect on the tissue. We determined that six subjects died when we administered the SK dose as intramedullary from "15000/kg." We thought that high mortality may be caused by the administration of the SK dose in the hospital, and we adjusted the dose. We determined that there was no mortality at a dose of SK given at 10,000 U/kg.

Hematomyelia triggers two distinct local responses. In the acute phase, a localized cellular response occurs, characterized by microglial cell proliferation. In the subacute phase, astrocyte proliferation results from hypertrophy and hyperplasia (2). Additionally, the second specific response involves the drainage of varying amounts of blood and blood products into the central canal of the spinal cord.

In our experimental study, histopathological examination on the first day revealed a high density of erythrocytes in the dorsal column, the presence of erythrocytes in the central canal, and tissue edema in both the control and experimental groups. By the 3rd day, erythrocyte levels began to decline, while polymorphonuclear leukocytes increased, and mononuclear leukocytes were observed, and edema became more pronounced. On the 7th day, there was a gradual reduction in erythrocyte density and edema, along with an expansion of the central canal, which contained blood and blood products proximal to the lesion site. By the 14th day, erythrocyte numbers continued to decrease, edema had resolved, and the central canal exhibited further widening at and proximal to the lesion site. Additionally, necrotic cells, blood products, and astroglial cell proliferation were detected within the central canal.

Our study also found enlargement of the central canal proximal to the lesion site. This enlargement can be attributed to several factors. In deep intramedullary hemorrhages during the acute phase, blood components drain into the central canal at varying levels within 2-6 hours after hemorrhage. In cases of superficial hemorrhage, secondary blood products

Table 4. Histopathological findings of the control group, classified into four grades based on follow-up periods of 1, 3, 7, and 14 days

Days	Erythrocyte count						Edema						Inflammatory cell count PNL (P) MN (m)						Astrogliotic cell count					
1	3	3	3	3	3	3	2	2	2	2	2	2	1 p	1 p	1 p	1 p	1 p	1 p	0	0	0	0	0	0
3	2	2	2	2	2	2	3	3	3	3	3	3	3 p	2 p	3 p	3 p	2 p	3 p	1	1	1	1	1	1
7	1	1	1	1	1	1	1	1	1	1	1	1	2 m	2 m	2 m	2 m	2 m	2 m	2	2	2	2	2	2
14	1	0	0	1	0	0	0	0	0	0	0	0	1 m	1 m	1 m	1 m	1 m	1 m	2	2	2	2	2	2

PNL: Polymorphonuclear leukocytes, MN: Monocyte

Table 5. Histopathological findings of the experimental group, categorized into four grades according to follow-up periods of 1, 3, 7, and 14 days

Days	Erythrocyte count						Edema						Inflammatory cell count PNL (P) MN (m)						Astrogliotic cell count					
1	3	3	2	3	3	3	2	1	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
3	2	2	2	2	2	2	3	3	3	3	3	3	1 p	1 p	1 p	1 p	1 p	1 p	1	1	1	1	1	1
7	1	1	1	1	1	1	1	1	1	1	1	1	1 m	1 m	1 m	1 m	1 m	1 m	1	1	1	1	1	1
14	1	1	0	0	1	1	1	1	1	1	1	1	1 m	1 m	1 m	1 m	1 m	1 m	1	1	1	1	1	1

PNL: Polymorphonuclear leukocytes, MN: Monocyte

such as fibrin and necrotic cells may be observed in the central canal within 24 hours post-hemorrhage.

The volume of the central canal increases due to the mass effect exerted by blood and secondary blood products. Additionally, the ciliary movement of ependymal cells occurs in a proximal direction, causing the central canal to remain open in the upper part of the spinal cord near the fourth ventricle, while it is closed in the lower region (5). Due to the toxic effects of secondary blood products, necrosis and structural degradation of ependymal cells occur, leading to disruption of the central canal. As a result, syrinx formation may develop rostral to the lesion site due to the accumulation of necrotic tissue, blood, or blood product drainage (2).

Following hemorrhage, coagulation and tissue organization take place. Within a few days, the coagulum undergoes fibrinolysis and liquefies. Masuda et al. (6) demonstrated that FA is absent during the initial days of intracerebral hematoma formation but begins to increase from day 3, reaching its peak around day 10.

They highlighted the significance of FA elevation in the early stages of hematoma formation, particularly in promoting hematoma lysis (7). Based on these findings, some researchers have conducted studies aimed at enhancing hematoma lysis.

Matsumoto and Hondo (8) utilized computed tomography-guided stereotactic injections into hematomas and reported successful outcomes following hematoma aspiration with urokinase administration.

Based on this approach, we experimentally induced hematomyelia in the dorsal column of the spinal cord using 0.1 cc of autologous blood obtained from the femoral artery, and applied SK, a first-generation fibrinolytic agent. Our study found no significant difference between the results of the control and experimental groups.

Concerns regarding the adequacy of the SK dose in pharmacotherapy include the lack of prior studies examining its effects on hematoma resorption, and axonal regeneration following FA in hematomyelia. Additionally, its short-term and single-use administration did not show sufficient impact on the recovery of sensory, autonomic, and motor functions after spinal cord injury (9). Consequently, the search for more effective pharmacological agents continues.

In our experimental study, we used a "frame" to position the injection site close to the clot and administered SK into the dorsal funiculus at the T4 spinal segment.

We did not perform surgical evacuation of the lysed hematoma; instead, we allowed for spontaneous absorption. The rate of FA may depend on the hematoma size. The hematoma's mass effect is significant, leading to ischemia and increasing secondary damage. Additionally, impaired circulation delays absorption and prevents inflammatory cells responsible for FA from reaching the injury site.

SEP has become a valuable tool for assessing spinal cord injury severity (10,11). Acute SEP measurements are effective for predicting recovery (12,13), while chronic SEP recovery has not been shown to correlate with functional improvement (12). In our study, SEP was used as a diagnostic tool to evaluate functional recovery following hematomyelia. However, we found no significant differences in the amplitude and latency values recorded electrophysiologically. There are certain electrophysiological limitations affecting SEPs' efficacy in pharmacotherapy. The disappearance of SEPs does not necessarily indicate the loss of axons, as conduction deficits can arise from multiple factors, including demyelination, changes in excitability at proximal and distal sites, and extracellular ion imbalances.

SEP is most effectively used during spinal surgery or experimental spinal cord injury studies (11), as it monitors acute axonal stress during these procedures. A decline in SEP potentials serves as a key criterion for alerting the surgeon to modify the procedure, helping to prevent postoperative neurological deficits. However, it is important to note that SEPs only assess dorsal spinal cord function. To achieve a more comprehensive evaluation of spinal cord integrity, improvements in motor evoked potential (MEP) monitoring are needed.

MEP amplitudes are highly variable, making their interpretation less reliable, as they tend to be significantly suppressed (14). In our experimental hematomyelia study, MEPs were not utilized due to their sensitivity to segmental excitability changes, and their incompatibility with anesthesia. Additionally, intraoperative SEPs do not always accurately reflect motor function (15,16).

Between 1980 and 1987, Blight and Young (17) conducted SEP studies on 500 patients with acute and chronic spinal cord injuries, aiming to establish correlations between SEP findings and neurological scores. In a spinal cord injury model, evaluating SEP changes over time may provide more valuable insights (17,18). Based on this, our study examined hematomyelia over specific time points—1, 3, 7, and 14 days—to assess the observed changes.

The presence of low-amplitude dorsal column potentials with delayed latencies in both the saline and SK-treated hematomyelia groups, without significant statistical differences from normal values, indicates a higher degree of axonal degeneration in this region.

Action potentials, which began appearing at low amplitudes by day 3, correlated with histopathological signs of tissue healing. However, dorsal column potential amplitudes in both the SK-treated and saline-treated groups were not significantly different on days 3, 7, and 14, suggesting that SK did not enhance axonal regeneration.

Study Limitation

The advantage of this study is that it was performed with experimentally homogeneous groups. the limitation could have been the addition of other markers in the activity in hematomyelia.

CONCLUSION

In our experimental study, the histopathological examination of the control and experimental groups, along with the statistical analysis of the electrophysiologically recorded amplitude and latency values, indicated that there was no observed benefit in terms of treatment outcomes. It was concluded that local SK treatment was not effective in hematomyelia.

Ethics

Ethics Committee Approval: Approval was obtained from the Surgical Medical Sciences Committee of Atatürk University Faculty of Medicine (decision no: 9, date: 04.05.1999).

Informed Consent: Experimental animal model study on the electrophysiological and histopathological effects of streptokinase in hematomyelia; therefore, informed consent could not be obtained.

Footnotes

Authorship Contributions

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Multicenter Acute Stroke Trial-Europe Study Group; Hommel M, Cornu C, Boutitie F, Boissel JP. Thrombolytic therapy with streptokinase in acute ischemic stroke. N Engl J Med. 1996;335:145-50. doi: 10.1056/NEJM199607183350301.
2. Milhorat TH, Adler DE, Heger IM, Miller JI, Hollenberg-Sher JR. Histopathology of experimental hematomyelia. J Neurosurg. 1991;75(6):911-5. doi: 10.3171/JNS.1991.75.6.0911.
3. Ginsburg HH, Shetter AG, Raudzens PA. Postoperative paraplegia with preserved intraoperative somatosensory evoked potentials. Case report. J Neurosurg. 1985;63(2):296-300. doi: 10.3171/JNS.1985.63.2.0296.
4. Fehlings MG, Tator CH, Linden RD. Origin of motor evoked potentials in the rat. Neurosurgery. 1989;24(2):299-300.
5. Li C, Houlden DA, Rowed DW. Somatosensory evoked potentials and neurological grades as predictors of outcome in acute spinal cord injury. J Neurosurg. 1990;72(4):600-9. http://doi.org/10.3171/JNS.1990.72.4.0600.
6. Masuda T, Dohrmann GJ, Kwaan HC, Erickson RK, Wollman RL. Fibrinolytic activity in experimental intracerebral hematoma. J Neurosurg. 1988;68(2):274-8. doi: 10.3171/JNS.1988.68.2.0274.
7. Acoustic neuroma and skull base surgery: proceedings of the 2nd International Conference on Acoustic Neuroma Surgery and 2nd European Skull Base Society Congress. 1996.
8. Matsumoto K, Hondo H. CT-guided stereotaxic evacuation of hypertensive intracerebral hematomas. J Neurosurg. 1984;61(3):440-8. doi: 10.3171/JNS.1984.61.3.0440.
9. Laffel GL, Braunwald E. Thrombolytic therapy. N Engl J Med. 1984;311(11):710-7. doi: 10.1056/NEJM198409133111105.
10. Julow J. Prevention of subarachnoid fibrosis after subarachnoid haemorrhage with urokinase. Scanning electron microscopic study in the dog. Acta Neurochir (Wien). 1979;51(1-2):51-63.
11. Koyanagi I, Iwasaki Y, Isu T, Abe H, Akino M, Kuroda S. Spinal cord evoked potential monitoring after spinal cord stimulation during surgery of spinal cord tumors. Neurosurgery. 1993;33(3):451-9. doi: 10.1227/00006123-199309000-00015.
12. Johnson Aj, Mccarty Wr. The lysis of artificially induced intravascular clots in man by intravenous infusions of streptokinase. J Clin Invest. 1959;38(9):1627-43. doi: 10.1172/JCI103941.
13. Wiman B, Collen D. Molecular mechanism of physiological fibrinolysis. Nature. 1978;272(5653):549-50. doi: 10.1038/272549a0.
14. Nath FP, Jenkins A, Mendelow AD, Graham DI, Teasdale GM. Early hemodynamic changes in experimental intracerebral hemorrhage. J Neurosurg. 1986;65:697-703. doi: 10.3171/JNS.1986.65.5.0697.
15. Chiappa KH, Ropper AH. Evoked potentials in clinical medicine (second of two parts). N Engl J Med. 1982;306(20):1205-11. doi: 10.1056/NEJM198205203062004.
16. Zileli M. Nöroşirurjide Elektrofizyolojik monitörleme teknikleri. EEG-EMG Derneği Yayınları. 1994.
17. Blight AR, Young W. Axonal morphometric correlates of evoked potentials in experimental spinal cord injury. Humana Press. 1990;87-113. doi: 10.1007/978-1-4612-0491-6_5.
18. Bracken MB, Shepard MJ, Hellenbrand KG, Collins WF, Leo LS, Freeman DF, et al. Methylprednisolone and neurological function 1 year after spinal cord injury: results of the national acute spinal cord injury study. J Neurosurg. 1985;63(5):704-13. doi: 10.3171/jns.1985.63.5.0704.

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Case Report

19

Amoxicillin-clavulanic Acid-induced Kounis Syndrome

Amoksisilin-klavulanik Asitin İndüklediği Kounis Sendromu

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ABSTRACT

Kounis syndrome (KS) is a condition in which an acute coronary syndrome occurs simultaneously with allergy, hypersensitivity, anaphylaxis, or anaphylactoid reactions caused by the activation of mast cells. The release of various mediators primarily histamine due to degranulation of mast cells plays a role in the pathophysiology of certain diseases. We report a case of KS with acute inferior ST-segment elevation myocardial infarction following oral use of an antibiotic containing amoxicillin-clavulanic acid.

Keywords: Amoxicillin, allergic myocardial infarction, acute coronary syndrome, Kounis syndrome

ÖZ

Kounis sendromu (KS) (alerjik miyokard infarktüsü), mast hücrelerinin aktifleşmesiyle oluşan alerji, hipersensitivite, anafilaksi veya anaflaktoid reaksiyonlar ile ilişkili akut koroner sendromun eş zamanlı meydana gelmesi durumudur. Patofizyolojide mast hücrelerinin degranülasyonuna bağlı olarak başta histamin olmak üzere çeşitli mediyatörlerin salınımı rol almaktadır. Amoksisilin-klavulanik asit içeren antibiyotiğin oral yoldan kullanımını takiben gelişen akut inferior ST-segment elevasyonlu miyokard infarktüsü tablosu ile başvuran KS olgusunu sunduk.

Anahtar Kelimeler: Amoksisilin, alerjik miyokard infarktüs, akut koroner sendromu, Kounis sendromu

INTRODUCTION

Kounis syndrome (KS) is a rare but clinically critical syndrome characterized by the development of coronary artery vasospasm, plaque rupture or stent thrombosis due to systemic inflammatory mediators during allergic or anaphylactic reactions. First described by Kounis (1) in 1991, it is also called "allergic myocardial infarction (MI)" and is usually associated with a pathophysiological process in which myocardial ischemia is triggered by histamine, tryptase, and other mediators released from mast cells. KS may present with symptoms of acute coronary syndrome in atopic individuals following exposure to various triggers such as drugs, food, and insect stings. In this case report, a clinically instructive case of the diagnosis and management of KS will be shared.

CASE REPORT

A 42-year-old male smoker with no known diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, or history of alcohol consumption was admitted to the emergency unit of our hospital with complaints of pruritus, rash, urticaria, dyspnea, and burning chest pain that started approximately 1 hour after taking 1000 mg amoxicillin-clavulanic acid orally. Vital signs were stable (temperature 36.6 °C, pulse rate 85 beats/minute, blood pressure 125/72 mmHg, SpO^2 98%, respiratory rate 12/minute) and he was rapidly administered diphenhydramine 45.5 mg intravenously, methylprednisolone sodium succinate 80 mg, and 500 mL saline. After the electrocardiogram showed ST segment elevation in leads DII, DIII, aVF, V5, and V6 and ST segment depression in leads D1, aVL, V1, and V2 (Figure 1), the patient was quickly taken to the catheterization laboratory for emergency selective coronary angiography with a preliminary diagnosis of acute inferior ST-elevation myocardial infarction (STEMI).

Right-left selective coronary angiography was performed (Figure 2). Normal epicardial coronary anatomy was found in the left circumflex artery and left anterior descending artery territory. In the right coronary artery (RCA) territory, 80% stenosis was observed in the distal lumen before crux. After the intracoronary administration of 400 micrograms glyceryl trinitrate, a complete patency was observed in the lumenogram. There was no evidence of coronary dissection, coronary plaque, or intracoronary thrombus in this region. This lesion in the RCA was evaluated as coronary

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vasospasm (Figure 2). The coronary angiography procedure was terminated. Ventriculography did not show any finding consistent with apical ballooning syndrome. In the anamnesis, it was learned that the patient had not experienced intense emotional stress recently. Myocarditis and tako-tsubo syndrome were ruled out in the differential diagnosis because of electrocardiography (ECG), transthoracic echocardiography, and auscultation findings (no friction rub). The patient was evaluated for antibiotic-associated coronary vasospasm and diagnosed with KS type 1 variant. ECG performed after coronary angiography showed a left ventricular ejection fraction of 55%. The left ventricular inferior wall was mildly hypokinetic, and no segmental motion defects were observed in the other walls. Valve structures and functions were reported as normal. In laboratory tests, the troponin was 388 ng/L (0-16), low-density lipoprotein was 105 mg/dL (20-100), thyroid-stimulating hormone was 0.396 mUI/L (0.34-5.6), alanine aminotransferase was 23 U/L (5-50), aspartate aminotransferase was 25 U/L (5-50), urea was 28 mg/dL (17-43), creatinine was 0.67 mg/dL (0.67-1.17), sodium was 134 mmol/L (136-146), potassium was 4.7 mmol/L (3.5-5.5), glucose was 98 mg/dl (74-106), c-reactive protein was 13.4 mg/L (0-5), erythrocyte sedimentation rate was 4 mm/h (0-15), hemoglobin was 15.2 g/dL (12.5-16.3).

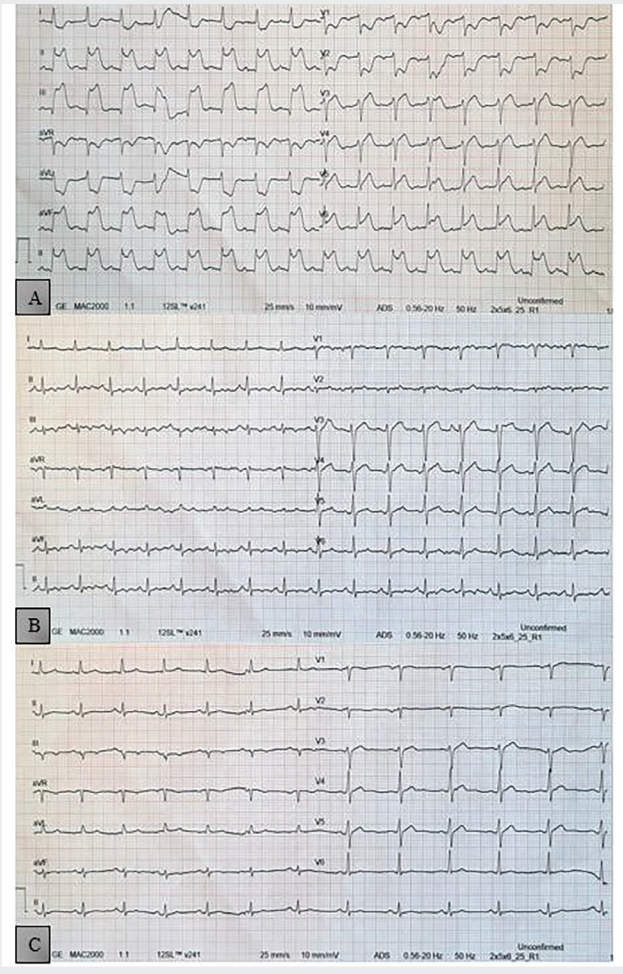

Figure 1. Electrocardiograms obtained at the time of presentation to the emergency department (A), 1 hour (B) and 24 hours (C) after the selective coronary angiography procedure

Our patient did not have chronic drug use, a history of previous allergic reactions, or any atopic diseases such as atopic dermatitis, asthma, and rhinitis. However, since KS develops as a result of an allergic reaction, the risk of recurrence may be high upon re-exposure to the triggering agent. The patient should be educated about exposure to the triggering agent. Treatment options such as antihistamines, corticosteroids, and epinephrine autoinjectors can be offered to the patient in case of recurrence.

After 48 hours of clinical follow-up, oral anti-histamine (fexofenadine 180 mg/day), calcium channel blocker (dilazem 120 mg/day), and antibiotic (clarithromycin 1000 mg/day) treatments were prescribed, education was given about exposure to the causative agent, and the patient was discharged with healing. Informed consent was obtained from our patient.

DISCUSSION

KS is characterized by the simultaneous occurrence of acute coronary syndromes such as coronary spasm (type I variant), acute MI (type II variant), and stent thrombosis (type III variant) in the context of allergic or hypersensitivity reactions, including anaphylactic or anaphylactoid events (1-4). KS can be triggered by various drugs (aspirin, antihypertensives, corticosteroids, antibiotics and non-steroidal anti-inflammatory drugs), foods, environmental factors (insect stings, snake bites), and clinical conditions (1-4). KS is triggered by the release of inflammatory mediators including histamine, platelet-activating factor, arachidonic acid derivatives, neutral proteases, various cytokines and chemokines during the allergic activation process. The KS type I variant includes patients without atherosclerotic coronary artery disease who develop coronary artery spasm secondary to acute release of inflammatory mediators (1-4). The KS type II variant includes patients with atherosclerotic heart disease who develop MI in the background of coronary plaque rupture or erosion secondary to acute release of inflammatory mediators (1-4). The KS type III variant includes patients with prior percutaneous coronary intervention who present with stent thrombosis or stent restenosis following a severe allergic reaction (5).

The diagnosis of KS is based on clinical symptoms and signs as well as laboratory, ECG, echocardiographic, and angiographic evidence. The main clinical signs of KS are cardiac symptoms accompanied by allergic reactions (1-3). Acute chest pain, chest tightness, dysphagia, dyspnea, syncope, headache, weakness, nausea, vomiting, and skin itching are observed as clinical symptoms, whereas cold extremities, hypotension, pallor, tachycardia, skin flushing, bradycardia, cardiorespiratory

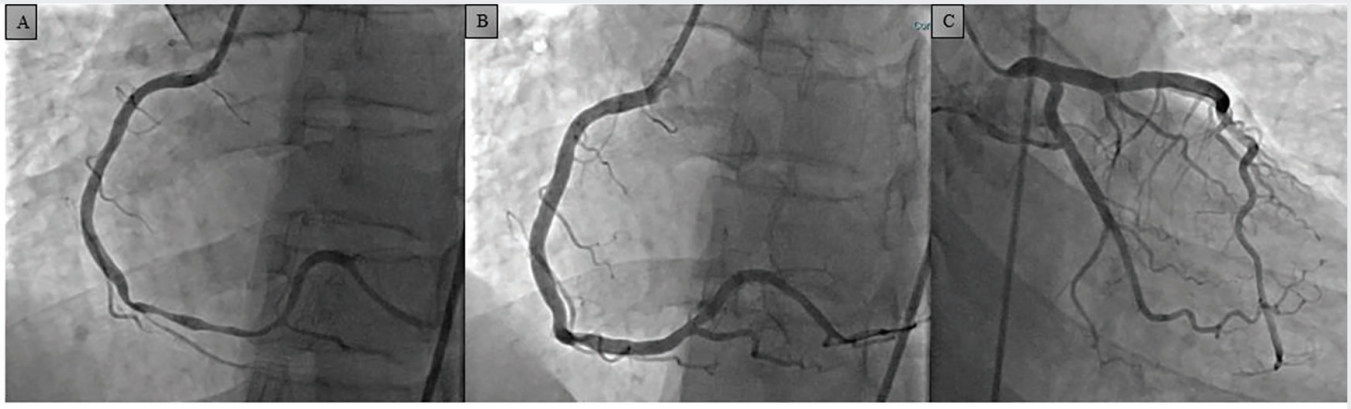

Figure 2. Selective coronary angiography recordings (A) Left oblique fluoroscopic image of severe vasospasm in the distal portion of the right coronary artery (RCA) (B) Left oblique fluoroscopic image showing complete resolution of this vasospasm after intracoronary nitrate administration (C) Right caudal fluoroscopic image showing normal left coronary system (LAD and LCx) LAD: Left anterior descending artery, LCx: Left circumflex artery

arrest, and sudden death may be observed as clinical findings (1-3). Various ECG changes including ST-segment elevation or depression, heart blocks, and cardiac arrhythmias are almost always associated with cardiac symptoms and signs. These symptoms/findings and ECG changes, which are often accompanied by allergic symptoms, aid in making the correct diagnosis (1-3).

Chatterjee et al. (4) recently presented a case of KS in a 44-year-old female patient who presented with sweating, dizziness, rash, chest tightness, and epigastric discomfort 1 hour after 625 mg of oral amoxicillin clavulanate, whose electrocardiogram revealed ST segment changes and troponin I elevation, and who had no comorbidities.

Chest pain in 63.6% and allergic reaction in 75.8% were the most common clinical findings in a review of 33 cases (median age 58 years, 81.8% male) by Wang et al. (5) who developed KS following amoxicillin use (6 cases (48.5%) amoxicillin, 7 patients (51.5%) amoxicillin-clavulanic acid) (4). In the diagnostic evaluation, troponin elevation was detected in 72.7%, ST-segment elevation, on electrocardiogram in 81.2%, and coronary artery thrombosis in 53.6% (4,5).

Ridella et al. (6) found skin reactions in 13 cases, respiratory symptoms in 7 cases, gastrointestinal system symptoms in 2 cases, chest pain in 11 cases, hypotension in 12 cases, ST segmen elevation on electrocardiogram in 16 cases, and troponin elevation in 10 cases (mean age 60 years, 76% male) who developed KS related to beta-lactam antibiotics (oral, intravenous or intramuscular route) (4). They found that all reactions occurred within 30 minutes and ST segment elevation was found in all patients, except one. In 10 cases, they found normal coronary arteries (4,6). In this series, as in our case, acute inferior STEMI was the most common type, and the RCA was found to be the coronary artery responsible for vasospasm.

Corticosteroids, antihistamines, and supportive treatment are usually sufficient in the KS type I variant. Calcium channel blockers may be used to eliminate coronary spasm. In the KS type II and III variant, appropriate acute coronary syndrome protocols need to be followed, in addition to the administration of antihistamines and steroids. In the KS type III variant, urgent aspiration of the thrombus and desensitization methods are required (4).

Our case describes type I KS following the use of oral amoxicillin clavulanic acid. This case highlights coronary vasospasm during an ongoing allergic reaction and its management with antihistamines, steroids, calcium channel blockers, and antiplatelet drugs.

The long-term follow-up of patients with KS should include careful monitoring for cardiovascular health and allergic reactions. Regular cardiac monitoring (echocardiography, biomarkers), education on avoiding triggering allergens, and allergic prophylaxis when necessary are important. With a multidisciplinary approach, it is important to ensure the cooperation of cardiology and allergy specialists.

In conclusion, in addition to clinical, ECG, and laboratory indicators of acute myocardial ischemia, patients presenting with systemic allergic reactions should be evaluated for the possibility of MI.

CONCLUSION

During allergic or anaphylactic shock reactions following the use of amoxicillin-clavulanic acid, it should be considered that KS may develop in the presence of symptoms suggestive of acute coronary syndrome, such as (chest pain, shortness of breath) electrocardiogram changes/or elevated levels of markers of myocardial damage (troponin). Therapeutic management of KS

requires simultaneous treatment of cardiac and allergic symptoms.

Although KS is a rare entity, its development in our case after an oral antibiotic, commonly used in community-acquired infections, suggests that this syndrome is a diagnosis that should be considered in clinical practice.

Ethics

Informed Consent: Informed consent was obtained from our patient.

Footnotes

Author Contributions

Surgical and Medical Practices: İ.K., H.C., B.C.K., M.E., Concept: İ.K., H.C., B.C.K., M.E., Design: İ.K., H.C., B.C.K., M.E., Data Collection or Processing: İ.K., H.C., B.C.K., M.E., Analysis or Interpretation: İ.K., H.C., B.C.K., M.E., Literature Search: İ.K., H.C., M.E., Writing: İ.K., M.E.

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REFERENCES

1. Kounis NG. Coronary hypersensitivity disorder: the Kounis syndrome. Clin Ther. 2013;35(5):563-71. doi: 10.1016/j.clinthera.2013.02.022.
2. Boarescu I, Boarescu PM. Drug-induced myocardial ınfarction: a review of pharmacological triggers and pathophysiological mechanisms. J Cardiovasc Dev Dis. 2024;11(12):406. doi: 10.3390/jcdd11120406.
3. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and the rapeutic management. Clin Chem Lab Med. 2016;54(10):1545-59. doi: 10.1515/cclm-2016-0010.
4. Chatterjee S, Paranjape S, Singh G. Kounis syndrome after oral amoxicillin clavulanate. Int J Appl Basic Med Res. 2025;15(1):66-8. doi: 10.4103/ijabmr.ijabmr_461_24.
5. Wang C, Zhou Y, Fang W, Li Z, Zhao S. Clinical features, diagnosis and management of amoxicillin-induced Kounis syndrome. Front Pharmacol. 2022;13:998239. doi: 10.3389/fphar.2022.998239.
6. Ridella M, Bagdure S, Nugent K, Cevik C. Kounis syndrome following beta-lactam antibiotic use: review of literature. Inflamm Allergy Drug Targets. 2009;8(1):11-6. doi: 10.2174/187152809787582462.